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NATIONAL GUIDELINE CLEARINGHOUSE

General

Guideline Title

Osteoporosis: diagnosis, treatment, and fracture prevention.

Bibliographic Source(s)

Medical Services Commission. Osteoporosis: diagnosis, treatment and fracture prevention. Vancouver (BC): British Columbia Medical Services Commission; 2011 May 1. 15 p. [41 references]

Guideline Status

This is the current release of the guideline.

Recommendations

Major Recommendations

Step 1: Assessment of Risks of Osteoporosis or Fracture

There are two aspects of risk that can be explored by identifying known risk factors:

Risk of developing osteoporosis (OP)
Risk of fracture within 10 years

Risk of Developing Osteoporosis

Family History	Parental history of hip fracture
Medical History	• Advanced age • Frailty* • Hyperthyroidism (including iatrogenic) or hyperparathyroidism • Celiac and other malabsorption syndromes • Bone mass index (BMI) <20 kg/m^2 or weight loss • Medication history, particularly chronic glucocorticoid use** (see Appendix A in the original guideline document) • Rheumatoid arthritis • Chronic liver or kidney disease

For Men	Androgen deficiency (primary or secondary)
For Women	• Estrogen deficiency (primary or secondary) • Early menopause (<45 years), including surgical • Cessation of menstruation for 6-12 consecutive months (excluding pregnancy, menopause or hysterectomy)
Lifestyle	• Smoking (current or former) • Daily alcohol consumption >3 units (1 unit = 5 oz wine, 1.5 oz spirits, 12 oz beer) • Caffeine intake >4 cups/day • Inadequate calcium and vitamin D intake • Lack of sunlight exposure (may cause vitamin D deficiency) • Prolonged immobility and lack of weight-bearing exercise

* See www.BCGuidelines.ca – *Frailty in Older Adults – Early Identification and Management* for definition
** i.e., ≥3 months (consecutive) therapy at a dose of prednisone ≥7.5 mg per day or equivalent

Calculate the 10-year Fragility Fracture Risk

The fracture risk of a patient can be estimated as Low (<10% in next 10 years), Moderate (10 - 20% in next 10 years), or High (>20% in next 10 years) using known risk factors and a clinical assessment tool. There are two tools available to calculate 10-year fracture risk. One is the FRAX® (see Appendix C - Using the FRAX® Calculator to Assess Absolute Fracture Risk in the original guideline document), developed by the World Health Organization (WHO), and the other is produced by the Canadian Association of Radiologists and Osteoporosis Canada (CAROC).

FRAX®* employs a web-based (www.shef.ac.uk/FRAX) calculator that includes a number of risk factors, including bone mineral density (BMD) which is optional. The CAROC paper-based risk table takes into account age, sex, fracture history, and glucocorticoid use to determine a ten-year absolute risk of all osteoporotic fractures, but BMD is required to calculate risk.

* Although the FRAX® tool has been developed for prognosis and is not prescriptive, this guideline suggests the use of a tool to identify all risk groups for whom treatment will depend on individual clinical parameters and specific therapeutic indications listed in Steps 3 and 4 (e.g., age, previous vertebral fracture, T score, where appropriate).

Falls and the Risk of Fracture (also see "Falls Prevention Strategies," below)

Over and above the risk of OP, other clinical factors predict those at increased risk of fracture, including:

Previous fragility fracture:

- Fractures sustained in falls from standing height or less, in which bone damage is disproportional to the degree of trauma. Includes vertebral compression fractures not attributable to previous major trauma, which may be suggested by height loss.
- Where other disease has been ruled out, patients with low trauma fragility fractures may have OP and are at high risk of other fragility fractures within 10 years.
- Fractures of the hip, vertebra, humerus, and wrist are most closely associated with OP and increased future fracture risk whereas those of the skull, fingers, toes, and patella fractures are not.

A fall in the last year

High risk of falling as determined by:

- Physical frailty or significant weight loss (loss of muscle mass). Refer to www.BCGuidelines.ca - *Frailty in Older Adults – Early Identification and Management*
- A global assessment of functional mobility like the timed "Up and Go" test
- Poor strength
- Balance problems
- Gait problems
- Dizziness
- Poor vision
- Psychotropic medications

- Cardiac insufficiency
- Urinary frequency and toileting issues
- Other validated tests

Step 2: Risk Stratification

Levels of Risk

Fracture risk estimation, using known risk factors and a clinical assessment tool, can be used to categorize patients as Low (<10% in next 10 years), Moderate (10 – 20% in next 10 years) or High (>20% in 10 years) fracture risk.

Risk Stratification Using Dual-Energy X-Ray Absorptiometry BMD

BMD is not indicated unless patients (men and women) are age >65 years, at moderate risk of fracture (10 - 20% 10-year risk), and results are likely to alter patient care. There has been a shift away from BMD and towards emphasizing multivariate fracture risk using a risk calculation model (FRAX® or CAROC). BMD is not recommended to be used alone as it explains only a portion of fracture risk. If a clinical risk assessment tool suggests moderate fracture risk category, consider BMD testing to further stratify risk and guide treatment; if high risk, consider treatment.

BMD is NOT indicated for:

- Investigation of chronic back pain
- Investigation of exaggerated dorsal kyphosis (fractures are best excluded by radiography)
- Screening women aged <65 years, unless significant clinical risk factors have been identified
- Part of a routine evaluation around the time of menopause
- Confirmation of OP when a fragility fracture occurs

T-score classification (number of standard deviations above or below the mean peak BMD):

- *Normal*: T is -1 and above
- *Osteopenia*: T is -1.1 to -2.4
- *Osteoporosis*: T -2.5 and below
- *Established or severe OP*: T is -2.5 or below and one or more prevalent low-trauma fractures

Dual-energy X-ray absorptiometry (DXA) is a quantitative test and it requires careful quality assurance. Structural abnormalities, positioning, artifacts (e.g., body weight), and analysis can significantly affect results.

Laboratory Testing (Bone Turnover Markers and Vitamin D)

Indications: Blood tests are not indicated to make an OP diagnosis or determine risk. Blood tests are only useful to establish or to rule out secondary causes of OP. Refer to *Appendix B - Testing for Suspected Secondary Causes of OP in Selected Patients* in the original guideline document.

Bone turnover markers: At present no single or combined assay is recommended except in specific circumstances. Assays have a proven use in research studies involving large samples but they are complex and variation is too great to be useful at the individual level.

Vitamin D: Routine testing is not required to diagnose OP or before/after starting vitamin D supplementation. Refer to www.BCGuidelines.ca - *Vitamin D Testing Protocol*.

Step 3: Lifestyle Advice (Regardless of Risk Level)

Nutrition: Help reduce fracture risk via adequate daily calcium and vitamin D. Note: doses recommended below for calcium and vitamin D represent total intake from diet and supplements.

- Calcium: Recommend 1000-1200 mg elemental calcium per day including supplements, if necessary. See OP *Patient Guide* (see the "Patient Resources" field). Advise patients not to exceed recommended amounts, as evidence does not support higher doses of calcium supplementation. In addition, a 2010 meta-analysis reported an increase in myocardial infarction in men and women given calcium supplementation (i.e., ≥500 mg elemental calcium per day) versus placebo. Note: this meta-analysis studied calcium supplementation alone and not in combination with vitamin D and the increased risk was associated with dietary intakes of greater than 800 mg (approximately) elemental calcium per day.
- Vitamin D: Recommend 800-1000 IU per day of vitamin D_3, including supplements if necessary, to adults over the age of 50. Higher doses

(i.e., 2000 IU per day) may be needed in some cases and are considered safe. See Patient Guide (see the "Patient Resources" field) and www.BCGuidelines.ca - *Vitamin D Testing Protocol*.
- Protein: Recommend an adequate intake of dietary protein (1g/kg/day).

Exercise: Regular weight-bearing and muscle-strengthening reduce the risk of falls and fractures by improving agility, strength, posture, and balance, as well as general health benefit.

Smoking: Tobacco products are detrimental to the skeleton as well as to overall health.

Alcohol: Intake of 3 or more units (5 oz wine, 1.5 oz spirits, 12 oz beer) per day is detrimental to bone health and increases the risk of falling.

Step 4: Therapy

Falls Prevention Strategies

Falls prevention is the first line of treatment (versus OP medications) for those at high risk for falling.

Table: Items to Identify Falls Risk and Reduce Falls (review with patient at least annually)

- Ask about falls in the past year
- Assess the time taken to stand from sitting
- Assess muscle strength, balance, and gait by watching the patient walk and move
- Check and correct postural hypotension and cardiac arrhythmias
- Evaluate any neurological problems
- Review prescription medications that may affect balance
- Provide a checklist for improving safety at home, i.e., The Safe Living Guide-A Guide to Home Safety for Seniors, www.phac-aspc.gc.ca

Consider referral to geriatric medicine, a falls prevention program, homecare, occupational therapy, or physical therapy.

Pharmacological Therapy

See also *Appendix D - Pharmacological Therapy for Osteoporosis* in the original guideline document.

Medications may be recommended, depending on fracture risk assessment. Manage based on degree of risk:

- *Low risk*: Generally require lifestyle advice and daily intake of calcium and vitamin D.
- *Moderate risk*: Medication is usually not necessary but can be considered in addition to lifestyle advice and adequate daily intake of calcium and vitamin D. When considering medications, take into account patient preference and additional clinical risk factors (see below).

Table: Additional Clinical Risk Factors

- Vertebral fractures (>25% height loss with end-plate disruption)
- Lumbar spine BMD T-score that is significantly worse than hip BMD T-score
- Men receiving androgen deprivation therapy for prostate cancer
- Women receiving aromatase inhibitor therapy for breast cancer
- Long-term or repeated systemic corticosteroid use (oral or parenteral) that does not meet the conventional criteria for recent prolonged systemic corticosteroid use (i.e., ≥3 consecutive months) therapy at a dose of prednisone ≥7.5 mg per day or equivalent)
- Recurrent falls

- *High risk*: Consider medication in addition to lifestyle advice and adequate daily intake of calcium and vitamin D. Patients with hip and other fragility fractures are considered to be high risk. Individuals can be considered as candidates for medication after implementing fall prevention strategies and providing lifestyle advice (see Step 3, above).

OP medications available in Canada include (alphabetically): alendronate, calcitonin, denosumab, estrogens (with or without progesterone), etidronate, raloxifene, risedronate, teriparatide, and zoledronic acid. Data are insufficient to determine if one drug class is superior to another for fracture prevention. Medication adherence (compliance and persistence) is required for fracture reduction, yet rates of adherence to OP treatments are low.

- Consider barriers to adherence including mode of administration, dosing regimens, side effects, and cost (see *Appendix D - Pharmacological Therapy for Osteoporosis* in the original guideline document).
- Combine adequate calcium and vitamin D with all pharmacological treatments (see Step 3: Lifestyle Advice, above). For information regarding PharmaCare coverage of these medications please refer to Appendix D in the original guideline document.

Bisphosphonates

These drugs preserve bone by decreasing rate of bone turnover and enhancing bone mineralization. To date, this class of drugs (specifically alendronate, risedronate, and zoledronic acid) has the largest body of randomized controlled trial evidence for osteoporosis. Superiority of one bisphosphonate over another has not been conclusively shown. Most studies have been in post-menopausal women and the optimal duration of therapy is unknown (to date most studies, with fractures as an endpoint, have had an average five years duration).

Bisphosphonates	Points to Consider
Alendronate (oral) & Risedronate (oral)	• Post-menopausal women: prevents vertebral, non-vertebral, and hip fractures • Men: Some evidence of decreased risk of vertebral fractures; some evidence of increased hip bone density, but no significant hip fracture reduction • Glucocorticoid induced osteoporosis (GIO): Some evidence of decreased vertebral fracture risk
Etidronate (oral)	• Post-menopausal women: prevents vertebral fractures • GIO: maintains BMD in GIO although data is limited; Health Canada approved indication is for GIO prevention only (not treatment)
Zoledronic acid (intravenous)	• Post-menopausal women: prevents vertebral, non-vertebral, and hip fractures • Men: Data is limited; Some evidence of decreased risk of vertebral and non-vertebral fractures (study included those with prior hip fracture and only 24% men) • GIO: maintains BMD • Cost effectiveness may limit use • Consider for high-risk patients who are unable to tolerate oral therapy or have poor adherence

Selective Estrogen Receptor Modulators (SERMs) (Raloxifene)

SERMs can act as estrogen agonists or antagonists. Raloxifene acts as an estrogen agonist on bone tissue. The estrogenic effects of raloxifene on bone in postmenopausal women decrease bone turnover.

Drug	Points to Consider
Raloxifene (oral)	• Post-menopausal women: reduces the incidence of vertebral fractures • May be considered in post-menopausal women who are unable to tolerate bisphosphonates and have no history of thromboembolic disease • Caution: Significantly increases the risk of venous thromboembolic disease and stroke

Receptor Activator of Nuclear Factor-kB (RANK) Ligand Inhibitor

Denosumab is an injectable monoclonal antibody to the receptor activator of nuclear factor-kB ligand (RANKL). It inhibits bone resorption by osteoclasts by blocking the interaction between RANKL and its receptor RANK on the surface of osteoblasts.

Drug	Points to Consider
Denosumab (subcutaneous)	• Post-menopausal women: prevents vertebral, non-vertebral, and hip fractures • Cost and lack of long term safety data may limit use

Synthetic Parathyroid Hormone

Teriparatide is an anabolic agent that improves bone quality, quantity, and increases bone strength.

Drug	Points to Consider
Teriparatide (subcutaneous)	• Post-menopausal women: prevents vertebral and non-vertebral fractures in postmenopausal women with severe OP • Men: increases BMD; currently no fracture data available • GIO: Some evidence of benefit in the treatment of GIO • Cost and need for daily subcutaneous injection may limit use • Consider for patients at increased risk of fracture or lack of response to other therapies • Maximum lifetime exposure is 24 months • Bisphosphonates must be discontinued prior to treatment • Gains in BMD decline once treatment with teriparatide is discontinued; consider anti-resorptive therapy after completing treatment course

Calcitonin Peptides

Calcitonin salmon is an inhibitor of bone resorption; available in parenteral and nasal spray formulations. Although calcitonin does not build bone, in women >5 years beyond menopause, it appears to slow bone loss and increase spinal bone density.

Drug	Points to Consider
Calcitonin (nasal)	• Post-menopausal women: Reduces incidence of vertebral fractures; however evidence for benefit is limited • Consider as an alternative when other more effective drugs cannot be used • Effective in decreasing acute pain associated with vertebral osteoporotic fractures • Calcitonin injection is currently not approved for the treatment of OP; it is sometimes prescribed for patients who have pain due to acute vertebral fractures (See *Appendix D - Pharmacological Therapy for Osteoporosis* in the original guideline document) • Nasal route of administration has the most data for use in OP and is more commonly used due to convenience and tolerability

Hormone Replacement Therapy (HRT) (estrogen with or without progesterone)

HRT is primarily indicated for the management of moderate to severe menopausal symptoms in women. A beneficial effect has been seen on BMD and fracture risk due to the significant anti-resorptive activity of estrogen.

Drug	Points to Consider
HRT (oral or transdermal)	• Post-menopausal women: Shown to prevent vertebral, hip and non-vertebral fractures • Is not recommended for the sole indication of OP prevention and for long term use for this indication; consider benefits versus risks (See *Appendix D - Pharmacological Therapy for Osteoporosis* in the original guideline document) • May be appropriate for OP prevention when it is already being used for the management of menopausal symptoms

Drug	Points to Consider

Step 5: Monitoring

Clinical Re-assessment

Re-assess patients as clinically indicated to monitor side effects, compliance, height loss, incident fractures, and risk of falls, which may alter patient management.

Follow-up BMD Measurements

There is insufficient evidence to recommend a testing frequency for patients not taking OP medications. Based on a patient's risk profile, BMD retesting may be indicated in 3-10 years.

For patients on OP medication, repeat BMD examinations are not justified based on current evidence. If a BMD is to be done, any changes would be difficult to detect prior to 3 years. Consider more frequent testing in specific high risk situations (e.g., multiple risk factors, or receiving ≥7.5 mg prednisone daily or its equivalent for 3 months consecutively who require a baseline examination and repeat scans at 6-month intervals while on treatment).

Women >65 years will usually lose bone. A stable BMD value on treatment may reflect successful treatment and appreciable decreases in fracture risk may accompany minor increases in BMD. Minor increases in BMD may also be due to testing variance. Ideally, any follow-up BMD testing is recommended to be done on the same DXA machine and at the same time of year.

Clinical Algorithm(s)

A clinical algorithm on recommendations for evaluation and management of osteoporotic and fragility fracture risk is provided in the original guideline document.

Scope

Disease/Condition(s)

Osteoporosis and related fractures

Guideline Category

Diagnosis

Management

Prevention

Risk Assessment

Treatment

Clinical Specialty

Family Practice

Geriatrics

Internal Medicine

Intended Users

Physicians

Guideline Objective(s)

To summarize current recommendations for risk estimation, diagnosis, prevention, and treatment of osteoporosis and related fractures in a general adult population (age 19+ years)

Target Population

General adult population (age 19+ years)

Interventions and Practices Considered

Assessment/Diagnosis

1. Risk assessment for osteoporosis or fracture using the FRAX® calculator or Canadian Association of Radiologists and Osteoporosis Canada (CAROC) risk table
2. Risk stratification
3. Dual-energy X-ray absorptiometry (DXA) bone mineral density scan (as indicated)
4. Medical history
5. Laboratory testing of bone turnover markers and vitamin D (considered but not recommended for diagnosis or risk assessment)
6. Clinical re-assessment and monitoring as indicated

Treatment

1. Lifestyle advice on exercise; calcium, vitamin D, and protein intake; smoking cessation; and alcohol intake
2. Falls prevention strategies
3. Pharmacological therapy
    - Bisphosphonates (alendronate, etidronate, risedronate, zoledronic acid)
    - Selective estrogen receptor modulators (SERMs) (raloxifene)
    - Receptor activator of nuclear factor-kB (RANK) ligand inhibitor (denosumab)
    - Synthetic parathyroid hormone (teriparatide)
    - Calcitonin
    - Hormone replacement therapy (HRT) (estrogen with or without progesterone)

Major Outcomes Considered

- Risk of developing osteoporosis (OP)
- Risk of fracture within 10 years
- Risk of falling
- Medication side effects

Methodology

Methods Used to Collect/Select the Evidence

Searches of Electronic Databases

Description of Methods Used to Collect/Select the Evidence

The systematic literature follows the Oxford Centre for Evidence-based Medicine - Levels of Evidence (March 2009) document methodology. Evidence was obtained through a systematic review of peer-reviewed literature (up to 2010) using the databases MEDLINE, PubMed, EBSCO, Ovid, and the Cochrane Collaboration's Database for Systematic Reviews. Clinical practice guidelines from other jurisdictions for osteoporosis were also reviewed (up to 2009).

Number of Source Documents

Not stated

Methods Used to Assess the Quality and Strength of the Evidence

Not stated

Rating Scheme for the Strength of the Evidence

Not applicable

Methods Used to Analyze the Evidence

Review of Published Meta-Analyses

Systematic Review

Description of the Methods Used to Analyze the Evidence

Not stated

Methods Used to Formulate the Recommendations

Expert Consensus

Description of Methods Used to Formulate the Recommendations

Not stated

Rating Scheme for the Strength of the Recommendations

Not applicable

Cost Analysis

The guideline developers reviewed published cost analyses.

Method of Guideline Validation

External Peer Review

Internal Peer Review

Description of Method of Guideline Validation

This guideline was developed by the Guidelines and Protocols Advisory Committee, approved by the British Columbia Medical Association, and adopted by the Medical Services Commission.

Evidence Supporting the Recommendations

Type of Evidence Supporting the Recommendations

The type of supporting evidence is not specifically stated for each recommendation.

Benefits/Harms of Implementing the Guideline Recommendations

Potential Benefits

- Accurate diagnosis and appropriate treatment of osteoporosis
- Effective prevention of fractures

Potential Harms

Side effects for medication are listed in *Appendix D - Pharmacological Therapy for Osteoporosis* in the original guideline document.

Calcium

A 2010 meta-analysis reported an increase in myocardial infarction in men and women given calcium supplementation (i.e., ≥500 mg elemental calcium per day) versus placebo. Note: this meta-analysis studied calcium supplementation alone and not in combination with vitamin D and the increased risk was associated with dietary intakes of greater than 800 mg (approximately) elemental calcium per day.

Contraindications

Contraindications

- *Alendronate* is contraindicated in patients with renal impairment (i.e., creatinine clearance [CrCl] <30 mL/min) or hypocalcemia.
- *Teriparatide* is contraindicated in patients with severe renal impairment or hypercalcemia and during pregnancy
- *Raloxifene* is contraindicated in pregnancy, and in patients with a history of venous thromboembolic events (VTE).
- *Denosumab* is contraindicated in patients with hypocalcemia.
- *Conjugated estrogen* is contraindicated in patients with a history of thromboembolic events or breast cancer.

Qualifying Statements

Qualifying Statements

The Clinical Practice Guidelines (the "Guidelines") have been developed by the Guidelines and Protocols Advisory Committee on behalf of the Medical Services Commission. The Guidelines are intended to give an understanding of a clinical problem, and outline one or more preferred approaches to the investigation and management of the problem. The Guidelines are not intended as a substitute for the advice or professional judgment of a health care professional, nor are they intended to be the only approach to the management of clinical problems.

Implementation of the Guideline

Description of Implementation Strategy

An implementation strategy was not provided.

Implementation Tools

Chart Documentation/Checklists/Forms

Clinical Algorithm

Mobile Device Resources

Patient Resources

Quick Reference Guides/Physician Guides

For information about availability, see the *Availability of Companion Documents* and *Patient Resources* fields below.

Institute of Medicine (IOM) National Healthcare Quality Report Categories

IOM Care Need

Living with Illness

Staying Healthy

IOM Domain

Effectiveness

Patient-centeredness

Identifying Information and Availability

Bibliographic Source(s)

Medical Services Commission. Osteoporosis: diagnosis, treatment and fracture prevention. Vancouver (BC): British Columbia Medical Services Commission; 2011 May 1. 15 p. [41 references]

Adaptation

Not applicable: The guideline was not adapted from another source.

Date Released

2011 May

Guideline Developer(s)

Medical Services Commission, British Columbia - State/Local Government Agency [Non-U.S.]

Source(s) of Funding

Medical Services Commission, British Columbia

Guideline Committee

Guidelines and Protocols Advisory Committee

Composition of Group That Authored the Guideline

Not stated

Financial Disclosures/Conflicts of Interest

Not stated

Guideline Status

This is the current release of the guideline.

Guideline Availability

Electronic copies: Available in Portable Document Format (PDF) from the British Columbia Ministry of Health Web site .

Availability of Companion Documents

The following is available:

- Osteoporosis: diagnosis, treatment and fracture prevention. Summary of guideline. Victoria (BC): British Columbia Medical Services Commission; 2011 May 1. 2 p. Electronic copies: Available in Portable Document Format (PDF) from the British Columbia Ministry of Health Web site .

In addition, a link to the FRAX Calculator to Assess Absolute Fracture Risk is available in Appendix C in the original guideline document .

Patient Resources

The following is available:

- Osteoporosis and fracture prevention. A guide for patients. Victoria (BC): British Columbia Medical Services Commission; 2011 May. 3 p. Electronic copies: Available in Portable Document Format (PDF) from the British Columbia Ministry of Health Web site .

Please note: This patient information is intended to provide health professionals with information to share with their patients to help them better

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